REMARKS

Claims 47-58 are pending in this application. Claims 47-49 and 53-55 are amended above to clarify that the liquid that is applied to the biological sample in order to separate the embedding medium from the biological sample is an immiscible liquid. Claim 47 has been amended to broaden the claim by removing the recitation of the density of the immiscible liquid. No new matter has been added to the application by way of this amendment to the claims above.

The Examiner's claim objections and rejections are traversed or overcome as set forth below.

I. TRAVERSE OF THE ANTICIPATION REJECTIONS

The Examiner rejected pending application claims 47-58 under 35 U.S.C. 102(b) as being anticipated by Zhang et al. (WO 95/24498) or, in the alternative, by Wang et al. The Examiner also rejected claims 47-50, 52-56, and 58 for being anticipated by Key et al. (U.S. Patent No. 5,244,787), or, in the alternative, by Mueller et al.

The Applicants respectfully traverse each of the Examiner's anticipation rejections. In each of the grounds for rejecting application claims for being anticipated, the Examiner made the statement that "the transitional term 'comprising', is inclusive or open ended and does not exclude additional, un recited elements or method steps." The Applicant's agree that independent method claims 47 and 53 use the term "comprising". However, in order to anticipate, each claimed feature must be found identically in a single prior art reference. As will shown below, none of the prior art references cited by the examiner discloses the methods of the presently claimed invention whereby a non-organic liquid is used to separate heated embedding medium from a biological sample. Instead, each of the references teach what the Applicants have admitted is in the prior art – using organic solvents to dissolve and remove embedding medium from a sample. Moreover, the use of the term "comprising" in the claims does not alter the fact that the prior art fails to disclose at least this step of the claimed processes.

A. Zhang et al. Does Not Disclose Removing An Embedding Media From A Sample Using An Immiscible Liquid

According to the Examiner, Zang et al. teaches a method for removing wax-embedded (e.g. paraffin) sample from a slide by using the slide in temperature controlled baths operating at a range of 5 to 50°C and flowing a wash solution over the isolated specimen where the wash solution comprises a buffer and a detergent wherein the detergent is non-ionic.

The Examiner's anticipation rejection is premised on a faulty understanding of Zhang et al. Zhang et al. does not disclose the step of the claimed methods whereby an immiscible liquid (such as water) is applied to a biological sample, either before or after heating the biological sample in order to separate heated embedding medium from the biological sample.

The steps of the Zhang et al. reference recited by the Examiner in rejecting the claims for anticipation do not occur sequentially. In Zhang et al. the sample that is placed in the heated water bath is a "dewaxed" specimen that is free of embedding medium. Therefore, it is impossible to remove embedding medium from the sample in the water bath in Zhang et al. because the sample contains no embedding medium to remove.

A close review of the teachings of Zhang et al. confirms this conclusion. Zhang et al. is directed to "new dewaxing solvent compositions for removal of paraffin or other waxes from wax embedded biological specimens". (page 3, lines 5-6). At pages 11 and 12 of the reference – the pages cited by the Examiner as including the allegedly anticipated description – the reference states:

> The process is quite simple and involves contacting a wax-embedded specimen with a dewaxing composition of the invention to solublize the wax that impregnates the specimen prior to histochemical analysis such as immunostaining. The method optionally comprises a further step of contacting the dewaxed specimen immediately after dewaxing with an aqueous washing composition comprising detergent to remove residual dewaxing composition.

(emphasis added). The Zhang et al. reference continues on to teach that the dewaxing may occur temperatures in a range of 5° to 50° because the heating decreases processing time. (See page 11, lines 19-24). Page 12 of the reference teaches that the "the dewaxed specimen can be

contacted with an aqueous wash composition of the invention which comprises a detergent." (Emphasis added). Thus, the Zhang et al. reference can be fairly described as teaching:

- The use of an organic solvent to remove wax from a wax embedded sample;
- The use of heat during the dewaxing step; and
- Contacting the "dewaxed specimen immediately after dewaxing" with a detergent containing aqueous solution.

The Zhang et al reference does not teach the important and claimed steps of contacting a heated biological sample containing a melted embedding medium with an immiscible liquid to removing embedding medium from the biological sample. Moreover, the Zhang et al. does not teach that it is desirable to heat the biological sample to the point where the embedding medium becomes liquidified. For at least this reason, Zhang et al. reference does not anticipate any pending application claim.

B. Wang et al. Does Not Disclose Removing An Embedding Media From A Sample Using An Immiscible Liquid

The claimed invention is not anticipated by Wang et al. It is the Examiner's position that Wang et al. teaches methods for removing a paraffin embedded specimen from a slide by heating the paraffin to 60°C or higher and then washing the isolated sample in a solution containing a surfactant. The Examiner points to column 2, lines 39-46 of the reference as support for the anticipation rejection.

Once again, the Examiner appears to be combining steps of the prior art that do not occur sequentially in order to construct an anticipation rejection. The Examiner's analysis of Wang et al. is faulty, because the specimen in Wang et al. that is washed with the washing solution is free of embedding medium. Therefore, Wang et al. cannot anticipate the claimed invention because it does not disclose the claimed step of contacting a heated biological sample containing a melted embedding medium with an immiscible liquid in order to remove the embedding medium from the biological sample.

As noted above, independent claims 47 and 53 each include steps of heating a biological sample including embedding medium and then separating the heated embedding medium for the

biological sample with an immiscible liquid that is applied to the sample either before or after heating. It is, therefore a feature of every claim that the immiscible liquid (e.g., water) is used to separate the heated embedding medium from the biological sample. This claimed feature is missing from Wang et al. because Wang et al. does not disclose any situation where a heated biological that includes an embedding medium is contacted with an immiscible liquid.

In the Wang et al. reference, an immiscible liquid (such as water) is **not** used to remove liquefied embedding medium from a biological sample. Instead, in Wang et al., the tissue sample is contacted with water only after the embedding medium has been removed. At column 2, lines 39-45, Wang et al. teaches:

> In addition, the present invention provides a process for treating a paraffin-embedded tissue sample to be used for a gene analysis, which comprises heating an aqueous suspension containing a **deparaffinized** tissue sample obtained from a paraffin-embedded tissue sample and a surfactant having a protein-denaturational action, reacting the heat-treated aqueous suspension with a protease, and then precipitating nucleic acid from the resulting reaction solution.

(Emphasis added). This passage from Wang et al. discusses a step for treating a tissue sample with an aqueous solution after it has been deparaffinized. In contrast, the claimed invention is directed to a deparaffinization process in which an immiscible liquid is applied to the heated biological sample in order to "separate the liquidified embedding medium from the biological sample ...."

The only discussion is Wang et al. about removing paraffin from the paraffin embedded tissue is at column 4, lines 16-36. This excerpt from Wang et al. discloses "adding a water insoluble organic solvent to the paraffin-embedded tissue sample, stirring and shaking the resulting mixture, centrifuging the mixture, and discarding the supernatant to remove paraffin." (Emphasis added).

Claims 47-58 are directed to methods wherein an immiscible liquid is applied to a heated biological sample "to separate the liquidified embedding medium from the biological sample". In contrast, Wang et al. discloses using an organic solvent to remove an embedding media from a biological sample and thereafter exposing the "deparaffinized tissue sample" to heated aqueous solution. Wang et al. does not disclose the stop of separating an embedding medium from a heated biological sample with an immiscible liquid. Therefore, Wang et al. does not disclose every

feature of the claimed invention, and the reference cannot anticipate any application claims.

C. Key Does Not Disclose Removing An Embedding Media From A Sample Using An Immiscible Liquid

The claimed invention is not anticipated by Key et al. It is the Examiner's position that the Key et al. reference teaches a method for removing paraffin from a paraffin embedded specimen by heating the paraffin at a range of 55 to 60°C and then placing the isolated sample into water or appropriate aqueous solution such an ionic surfactant. As with Zhang et al. and Wang et al., Key et al. cannot anticipate the claimed invention because it does not disclose the claimed feature of applying an immiscible liquid to the biological sample to separate the heated or liquified embedding medium from the biological sample.

First and foremost, Key et al. is not directed to a process for deparaffinizing a biological sample. The vast majority of the Key et al. reference is directed to describing "an improved technique for immunological staining of formalin-fixed tissue." (Column 3, lines 52-44). The technique is performed on deparaffinized biological samples. Key et al. does, however, describe how formalin-fixed, paraffin-embedded tissue samples are deparaffinized in the following, single, short paragraph:

> typically paraffin is removed from the paraffin-embedded tissue, for example by melting the paraffin (which has a melting point of approximately 55°C - 60°C depending upon the type of paraffin) or dissolving the paraffin in the appropriate solvent such as chloroform or xylene.

The remainder of column 5 (column 5, lines 59-68 and column 6, lines 1-33) of Key et al., cited by the Examiner in support of the anticipation rejection of claims 47-50, 52-56 and 58 does not describe a deparaffinization process. Instead, the cited excerpt is directed to the "process of the present invention" which is immunological staining of an already deparaffinized sample. Thus, Key et al. is fairly understood to disclose removing paraffin from a paraffin embedded tissue by (1) heating a sample to melt the paraffin; or (2) by contacting the paraffin embedded sample with an organic solvent.

Key et al. does not disclose or suggest the claim steps of contacting a heated biological sample with an immiscible liquid to separate a liquidified or heated embedding medium from the biological sample and Key et al. cannot anticipate any application claim at least for this reason.

D. Mueller Does Not Disclose Removing Embedding Media From A Sample Using An Immiscible Liquid

Mueller et al. does not anticipate claims 47-50, 52-56 and 58 for precisely the same reasons the prior three references do not anticipate. It is the Examiner's position that the Mueller et al. reference teaches methods of removing paraffin wax from and embedded sample by heating paraffin to 56°C and then washing the isolated specimen with a buffered saline.

Mueller et al. does not disclose or suggest the claimed methods. The portion of Mueller et al. cited by the Examiner (page 8, lines 41-47 and page 12, line 8) does not anticipate the claimed invention. Page 8 of the Mueller et al. reference discloses prior art staining and states that:

> Paraffin treated tissue sections may be heat treated at about 56°C or the like, and then washed in xylene to remove (dissolve) the paraffin.

This excerpt of Mueller et al. discloses removing heated paraffin from a biological sample using an organic solvent – xylene. Mueller et al. goes on to disclose that the specimen can be rehydrated, but the rehydration occurs only after the heated paraffin is removed from the sample using xylene.

The xylene disclosed in Mueller et al. is an organic liquid and not an immiscible liquid such as is claimed in all the pending application claims. Thus, Mueller et al. does not anticipate any of the pending application claims because it does not disclose the step of applying an immiscible liquid to the biological sample to separate a liquidified or heated embedding medium from a biological sample.

II. TRAVERSE OF THE DOUBLE PATENTING REJECTION

The Examiner rejected claims 47-58 under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,544,798.

The Applicants have overcome this rejection by submitting a Terminal Disclaimer simultaneously with the filing of this Reply. A copy of the Terminal Disclaimer accompanies this Reply at Appendix A.

CONCLUSION

In view of the amendments and statements in favor of claim patentability presented above, it is believed that all pending claims 47-58 of this application are allowable and that all claim rejections and objections should be withdrawn. Favorable reconsideration and allowance of all application claims is, therefore, courteously solicited.

Respectfully submitted,

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APPENDIX A